

## SINGULARITIES: LANDMARKS ON THE PATHWAYS OF LIFE

This brief but deep book presents a sophisticated consideration of the key steps or bottlenecks that constrain the path to the origin and evolution of life. Christian de Duve, a pioneer of modern cell biology and Nobel laureate, gives in this book a contemporary response to Erwin Schrödinger's tremendously influential *What Is Life?*, which 60 years ago influenced many of the pioneers of molecular biology. Christian de Duve offers shrewd insights on the conditions that may have first called forth life and surveys the entire history of life, using as landmarks the many remarkable singularities along the way, such as the single ancestry of all living beings, the universal genetic code, and the monophyletic origin of eukaryotes. The book offers a brief guided tour of biochemistry and phylogeny, from the basic molecular building blocks to the origin of humans. Each successive singularity is introduced in a sequence paralleling the hypothetical development of features and conditions on the primitive earth, explaining how and why each transition to greater complexity occurred.

Christian de Duve is Andrew W. Mellon Professor emeritus at The Rockefeller University, Professor emeritus at the Catholic University of Louvain and Founder-Administrator of the Christian de Duve Institute of Cellular Pathology. In 1974 he was jointly awarded the Nobel Prize in Physiology or Medicine, with Albert Claude and George Palade, and still conducts groundbreaking research into the origins of life.

# Singularities

## LANDMARKS ON THE PATHWAYS OF LIFE

CHRISTIAN DE DUVE



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## Foreword

This book was not meant to happen. When I finished *Life Evolving* (de Duve, 2002), I resolved not to write another book. In that work, and in the three that preceded it (de Duve, 1984, 1991, 1995), I had written all I had to say on the subject of life, including its nature, origin, and evolutionary history, up to and beyond the advent of humankind, and even its cosmic significance. In fact, I made the embarrassing discovery, when called upon to reread some passages of these books, that I tended to repeat myself, sometimes using almost the same words – an ominous sign indeed.

I changed my mind and began writing this book when I discovered that, in trying to reach a wide readership, I had buried a number of scientific points that I felt to be significant and original within more general expositions designed for lay readers. The message I wished to convey had been blurred, even misinterpreted as reflecting the pursuit of an ideological agenda (Szathmary, 2002; Lazcano, 2003).

This realization has prompted me to clarify my thoughts, remove extraneous material, and formulate the result concisely for a scientifically literate readership. My aim is to reach not just my fellow biologists but all those scientists, from physicists, cosmologists, and geologists to naturalists and anthropologists, who share an interest in the place occupied by life, including our own, in the cosmos. For this purpose, I have, with

apologies to the experts, summarized once again the key features of life, much in the line of my earlier *Blueprint for a Cell* (de Duve, 1991), but this time with a focus on *singularities*, by which I mean events or properties that have the quality of singleness, uniqueness.

The history of life is marked by a large number of such singularities. All known living organisms, be they microbes, plants, fungi, or animals, including humans, are descendants from a single form of life. All are constructed with the same building blocks and combine these into their characteristic constituents by the same biosynthetic processes. All carry out the same metabolic reactions and rely on the same mechanisms to derive energy from their environment and convert it into useful work. There are differences, of course, depending on the nature of the substances utilized, on the source of energy, and on the kind of work performed. But the basic processes are the same. All known living organisms use the same genetic language; they obey the same base-pairing rules and, with rare deviations of recent occurrence, conform to the same genetic code. Behind the enormous diversity of the biosphere, there clearly lies a single, fundamental blueprint.

Considering later stages of evolution, we find that all eukaryotes are derived from a single ancestral cell. Similarly, land plants, fungi, and animals are each monophyletic, that is, offshoots of a single founding organism; so are the members of each class or family, as abundantly illustrated by cladistics and confirmed by molecular phylogenies.

Often taken more or less for granted, these singularities require an explanation. Looking for such an explanation may reveal some valuable facts concerning the nature of life, its origin, and its evolution. It may also help guide our explorations in search of signs of life elsewhere in our galaxy and beyond.

Such is the purpose of this essay. References to the literature are sparse and largely restricted to recent publications. By necessity, the book is rooted in biochemistry, molecular biology, and cell biology, but in a manner designed to make these disciplines accessible to any reader with some familiarity with the language of modern science and, perhaps, to encourage some to take a more active interest in the disciplines and to acquire

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the basic notions without which a true appreciation of the significance of life in the universe is not possible.

The book covers a wide area, exceeding by far the domain of my own competence. Several friends and colleagues have helped me make up to some extent for these deficiencies. In particular, Nicolas Glansdorff, Patricia Johnson, Antonio Lazcano, Harold Morowitz, Miklos Müller, Guy Ourisson, Andrew Rogers, and Günter Wächtershäuser have read all or part of the original manuscript and contributed valuable information, comments, criticisms, and suggestions. I am deeply grateful to them but must claim sole responsibility for the final text, including its mistakes and idiosyncrasies, especially in that I have not always followed the advice with which I was favored. I am also indebted to Jeffrey Bada, Johannes Hackstein, Arthur Kornberg, and William Martin for providing me with some of their recent publications. I owe a special debt of gratitude for the invaluable assistance of my friend Neil Patterson, who has, once again, waded through my prose and helped me trim it of unnecessary words and clarify its contents. I also acknowledge with thanks the efficient and constructive collaboration of Peter Gordon, Alan Gold, and their colleagues at Cambridge University Press and of Doug English at TechBooks. Also, I acknowledge with emotion the memory of my devoted and talented Karrie, who helped me in all my writings for more than thirty years.



## On Christian de Duve: An Editor's Appreciation

Art and science are all of a piece in the life and work of Christian de Duve. I have had the privilege of serving as his editor on five books in 25 years. I have dined with him at many tables, worked with him at many desks, and witnessed the passion and grace of his labor to understand how life works and how it came to be. In all this time and through all these tasks I have watched the force of his intellect convert to words on paper his deep knowledge and intuitive sense of the most basic biological processes, giving the reader sweeping views of life evolving from molecules to the millions of species with which we share this planet.

It all looks easy when the book is bound – his narrative unfolds in a compelling way, the argument grows in strength, a convincing theme emerges, and its variations weave across the pages with thrilling strength and subtlety – but I've been close enough to see how he does it, and it's hard work, strenuous and painstaking, the kind of slow and heavy effort that we sensibly call a labor of love. One would not do this work just for money; it's way too tough; or even for fame, often a more seductive lure. So it is love, I think, that drives de Duve to write these books, just as it was love (the love of truth, however corny that may sound) that kept him at the laboratory bench for more than five decades of exacting science. That's part of what I mean about "art and science"; both, when done at the highest level, produce a piercing effect on the human mind, an illumination.

## ON CHRISTIAN DE DUVE: AN EDITOR'S APPRECIATION

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I began my editorial work with de Duve in 1980. (By the way, my so-called *editorial work* must be seen as thin soup when placed against the power of his contributions; this is not a collaboration between equals, far from it.) He had decided to write a book based on his notes for the 1976 “Christmas Lectures on Science” at Rockefeller University, a book to be called *Guided Tour of the Living Cell*. At that time, my colleagues and I at W. H. Freeman – under the bright and enthusiastic guidance of our boss and mentor, Gerard Piel, President of the parent company, Scientific American – had just begun a new imprint, *Scientific American Books*, and a new series, the *Scientific American Library*. We launched the series with *Powers of Ten* (about the relative size of things in the universe) by Philip and Phyllis Morrison and Charles and Ray Eames. This book gives a wonderfully vivid look at the effect of adding a zero. In an exponential series of images and words, the Morrisons and the Eameses take you, one order of magnitude at a time, each on its own two-page spread, from a picnic in Chicago at  $10^1$  meters up to  $10^{25}$  meters (one billion light years), where space “looks” empty, and down to  $10^{-16}$  meters, the realm of quarks.

*Powers of Ten* was a big hit, and it set the intellectual mood and established standards of content and design that we would have to sustain in order to meet the goals set by Piel and his Board of Directors. Enter de Duve. As I say, he was already busy making his lecture notes into a book, not just a scholarly monograph of the sort that scientists of his stature produce routinely for their peers, but a more ambitious enterprise, a survey of the entirety of cell biology that was meant to catch the interest, and inform and entertain, ordinary folks in the open world, the *trade*, as they say in the publishing business. This was the sort of book we at Scientific American needed in order to match the marketing impact gained by *Powers of Ten*. But was this making sense? Who is de Duve? He’s in a white coat at Rockefeller University, a Nobel Laureate, a high-powered scientist whose native tongue is French, whose writings up to this point have been academic treatises on the biochemistry and bioenergetics of cellular transactions that only his sophisticated cohorts would trouble to read.

My colleagues and I met de Duve in his offices at Rockefeller University. We told him about our new series, walked away with a chunk of his manuscript, read it, saw that he had what it takes, signed him up, and then the action took off. This was a tiger, and he had *us* by the tail.

First-rate authors in the fields of science are particularly demanding, and for good reason. Science is not for the faint-hearted; scientists demand a lot from themselves and each other – acuity, rigor, integrity, and horrendously hard work – so they expect a publisher to do its tasks in like manner. Such authors, of course, are almost always disappointed, so it is no surprise that de Duve was promptly exasperated. We had assigned one of our most experienced editors, Patty Mittelstadt, to shepherd de Duve's project through the developmental process. Suffice it to say that, despite her muscular will and years of experience in the editorial trenches, de Duve managed to have her in tears on several occasions. A disputed semicolon could cause a storm.

Although our colleague did a strong, professional job under taxing circumstances, de Duve served, essentially, as his own developmental editor; and he worked with the artist, Neil Hardy, in so diligent and scrupulous a fashion that Hardy could render de Duve's "rough" sketches – remarkably clear delineations of molecular and cellular forms and interactions, all to scale, with exact bond lengths and angles, every image color-coded – without having to worry about accuracy. This "rough" art was correct.

It happens now and then that an author becomes a kind of gift to the publishing house, a performer of such astonishing ability that the publishing team – managers, editors, marketers – end up playing, are only allowed to play, a perfunctory role in the process. In a half-century of publishing, I've received just three such "gifts," at three separate houses: at W. A. Benjamin, Inc. (now Benjamin-Cummings) it was James D. Watson's *Molecular Biology of the Gene*; at Worth Publishers it was Albert Lehninger's *Biochemistry*; and at Scientific American Books it was de Duve's *Guided Tour of the Living Cell*. In each of these cases, the author gave so much skill and attention to details of content, level of discussion, writing style, illustrations, and all the other elements that shape such a book and determine its success that the publishing team had only to handle mundane procedures of copyediting, design, page layout, printing, binding, warehousing, marketing, shipping, billing, and collecting. These three books jumped off the shelves. They were bought, not sold. (In my experience, only the rigorous and brilliant Michael Munowitz has achieved this level of authorial perfection, and his gifts went to houses where I was not employed.)

"*Tour*" sold 70,000 copies in a couple of years, a best seller in the trade market for science books at this level, and it demonstrated de Duve's

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membership in that small and increasingly precious pantheon of contemporary scientists who have the rare ability to write for the general public. This is a serious talent, a critical contribution to cultures around the globe. We live in politics captured by *belief*. Belief is a golden virtue; merely by asserting beliefs one can win huge support in the American political system. But believing is easy, and knowing is hard, and it's knowing that matters most. Those scientists (Peter Atkins, Andrew Berry, Richard Dawkins, Christian de Duve, Jared Diamond, Michael Munowitz, Steven Pinker, Matt Ridley, Oliver Sacks, James D. Watson, Steven Weinberg, Edward O. Wilson, et al.) who can write with clarity and balance and evocative power about that which is so, about the nature of physical and biological reality, from matter and energy at the Planck length to the edge of the visible universe and beyond, who can show what we know and don't know and how knowing itself is achieved and how it must often be seen as tentative and open to question, those scientist-artists, for that's what they are, become an essential human resource, national treasures whose works help wean us from the comfortable obscurantism of convictions born of belief.

I didn't do much work on this first book by de Duve (my main contribution being the engagement of Malcolm Gear, the great American graphic designer, who invented the visual character of this two-volume work, a stunning physical object in its own right), but over the next many years Christian and I together devised what, for me, became a delightful set of editorial rituals. Three great de Duvian works emerged during this period: *Blueprint for a Cell* (Neil Patterson Publishers, 1988, an ephemeral imprint later purchased by Viacom and metabolized within the body of its huge and flourishing subsidiary, Prentice-Hall), *Vital Dust: Life as a Cosmic Imperative* (Basic Books, 1995), and *Life Evolving: Molecules, Mind, and Meaning* (Oxford University Press, 2003). There were lunches and dinners and wine and good cheer, during which outlines were discussed, schedules set, and contract terms constructed. There were our side-by-side examinations of my modest editorial adjustments, mostly removing Gallicisms, for he writes in French and English with equal facility, and sometimes an idiom from one would invade the other. And then there were the Nethen Episodes, week-long sessions of intensive, sharply focused concentration on a "final" manuscript, a wrap-up to ready the work for printing.

Nethen, just beyond the edge of Brussels, is de Duve's hometown, and it is here, in bucolic serenity, that the value of ritual is fully in evidence.

During these sessions, the daily regimen begins at 6 AM with about twenty minutes of swift swimming in the backyard pool. This is not fun; it's humorless aerobic effort, length upon length. Next comes breakfast served by Janine de Duve, his stylish, beautiful, and loving wife of 60 years, an accomplished artist and a woman of high intelligence and the native honesty to express her views with sharp, good-humored precision. Then it's upstairs to our respective stations; de Duve to his study, I to my room. We work separately until noon. Then lunch (and sometimes a walk in the woods), then work, again separately, until the late afternoon, when we meet to consider together what he's done and I've done. At last, cocktails at 6, dinner (always entirely satisfying, often amazing), then, oddly, an interlude of television – the news and, usually, a favorite quiz program broadcast from Paris – and so to bed.

This kind of clockwork action is highly productive and may well be a common procedure among research scientists. For de Duve, even now, in his 86th year, it seems essential; he has a driving need to be productive, to keep at it. But all is not severity and discipline. Every interlude between periods of hard work is a time of great pleasure for him. When he's in New York City (throughout most of his long career he has spent half of each year at Rockefeller University, NYC, and the other half at the de Duve Institute of Cellular Pathology, Brussels, Belgium), he walks briskly, weather be damned, from his apartment on Central Park West, across the park, and over to the shore of the East River, York Avenue and 66th street, and bounds up four flights of stairs to his office. This walk is savored: a time to think, a time to enjoy the physical patterns of life itself. Lunches and dinners are likewise times to satisfy his appetites for food and wine, laughter and conversation, and the enduring delight he finds in the company of friends and colleagues. He makes an excellent friend, and he is a friend to many.

This book, *Singularities*, he tells me is his swan song. But this can't be so. He told me that same thing two books ago, when he was beginning *Vital Dust*. How can we afford to let de Duve retire? In any case, such a condition in no way suits his nature, for which we must all be truly grateful.

Neil Patterson